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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,709	05/20/2005	Jens Damsgaard Mikkelsen	2815-0316PUS1	7585

2292 7590 04/27/2009  
BIRCH STEWART KOLASCH & BIRCH  
PO BOX 747  
FALLS CHURCH, VA 22040-0747

EXAMINER
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CORNET, JEAN P

ART UNIT	PAPER NUMBER
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4121

NOTIFICATION DATE	DELIVERY MODE
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04/27/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/535,709	<b>Applicant(s)</b> MIKKELSEN, JENS DAMSGAARD	
	<b>Examiner</b> JEAN CORNET	<b>Art Unit</b> 4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 April 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) 6-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>05/20/2005</u> .  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. This application for Patent entered the national stage in the United States of America under U.S.C. 371 from PCT/EP03/50860, filed 11/21/2003, which claiming benefit from Denmark application no. Denmark PA 50860, filed 11/21/2002. Claims 1-10 are pending.

### ***Priority***

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. All claims receive the benefit of said European application filing date.

### ***Information Disclosure Statement***

3. All references submitted on the IDS dated 01/05/2007 have been considered.

### ***Election/Restrictions***

4. Applicant's election without traverse of Group I, claims 1-5 in the reply filed on 04/06/2009 is acknowledged.

Claims 6-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected invention, there being no allowable generic or linking claims. Election was made **without** traverse in the reply filed on 04/06/2009

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Limitation "exposing the compound or selecting the compound" in claims 1, 4 and 5 render the claims unclear because the metes and bound of the claim cannot be determined. It is unclear as to whether or not the compound is referred to a GABA modulator.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuo-Fen et al (WO0105222) in view of Barbaccia (Stress and Neurosteroids in Adult and Aged Rats, Experimental Gerontology, Vol 33, Nos 7/8, pp. 697-712, 1998), both cited in the IDS.**

The instant application is drawn to a method of screening a GABA<sub>A</sub> receptor modulator for its potential as a sedative or anxiolytica, which comprises exposing the compound to a test animal by administration; and measuring the effect of the compound on the activity of the HPA axis.

As to claim 1-3, Kuo-Fen et al teaches a method for screening for compounds having an effect on the response of the hypothalamic-pituitary-adrenal axis (HPA) to stress, comprising the steps of

- a) administering said compound to a transgenic mouse with a disruption in at least one allele of the corticotrophin releasing factor receptor 2 (CRFR2),
- b) putting the said mouse in a stress-inducing situation,
- c) monitoring plasma levels of corticosterone and adrenocorticotrophic hormone (ACTH) in the mouse after administration, and
- d) comparing said levels to those said transgenic mouse not placed in a stress-inducing conditions (claim 12).

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compounds having a sedative effect in this model will induced less stress response in terms of increase corticosterone or ACTH release which are components of the HPA axis activity.

Although the instantly claimed invention differs in that the compounds have to be modulators of the GABA<sub>A</sub> receptor, It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute a GABA<sub>A</sub> receptor modulator when Kuo-Fen is taking in view of Barcaccia et al, Barbaccia suggests that modulators of GABA<sub>A</sub> receptors affect correspondingly the HPA axis and the behavioral correlates to acute stress (abstract), thus remedies the deficiency of Kuo-Fen.

One would have been motivated to do so, with reasonable expectation of success because barcaccia's teaching clearly suggests that the substitution would have been equivalent. The techniques and skill required to such substitution is conventional knowledge or well within the skill of ordinary artisan.

Kuo-Fen does not teach selecting the compound as a sedative drug candidate if the compound substantially stimulates the HPA axis as in claim 4 and selecting the compound as an anxiolytica drug candidate, if the compound substantially has no effect on the HPA axis as in claim 5.

As to claims 4 and 5, Barbaccia et al teaches modulators of GABA<sub>A</sub> receptors affect the HPA axis and the behavior correlates of acute stress (page 698 first

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paragraph and page 710 second paragraph). Barbaccia further teaches contrary to inhibitors, activators prevent the activation of the HPA axis, i.e reduce the plasma and brain neurosteroid, and induce less stress response. Modulators of GABA<sub>A</sub> receptors are generally known as anxiolytics and hypnotics (abstract)

It would have been prima facie obvious to one of ordinary skill in the art to combine the features of Barbarccia's reference with corresponding effect to the known screening method of Kuo-Fen to come to the solution proposed by the instantly claimed application by selecting compounds either as sedative drugs or anxiolytica drugs.

Because of the supporting features of the GABA<sub>A</sub> receptor modulators, the scope of the claims is embraced by the teaching of the cited references.

One would have been motivated to do so; with reasonable expectation of success because Barbaccia et al suggests that GABA<sub>A</sub> receptor modulators can be stimulated and activated.

All the critical elements required by the claims are obvious over the well taught and thus, the claimed subject matter is not patentably distinct over the prior art of the invention.

***In conclusion***

8. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Friday 7.30am-5.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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/JC/

/Patrick J. Nolan/

Supervisory Patent Examiner, Art Unit 4121